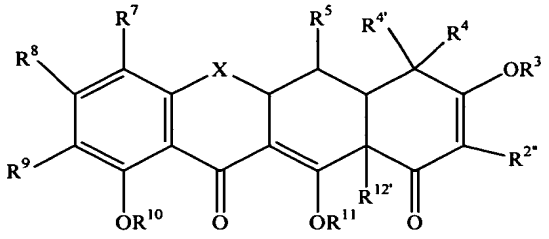
CLAIMS

1. A tetracycline compound of Formula I:



(I)

wherein:

X is $CHC(R^{13}Y'Y)$, $CR^{6'}R^6$, S, NR^6, or O;

$R^{2"}$ is $-C(=O)NR^2R^{2'}$, or –CN;

R^2, $R^{2'}$, R^{4a}, and R^{4b} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^3, R^{10}, R^{11}, R^{12}, and $R^{12"}$ are each independently hydrogen, alkyl, alkenyl, aryl, alkynyl, aralkyl, acetyl, alkylcarbonyl, alkenylcarbonyl, arylcarbonyl, alkynylcarbonyl, alkyloxycarbonyl, alkenyloxycarbonyl, alkynyloxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkynylaminocarbonyl, arylaminocarbonyl, alkylthiocarbonyl, alkenylthiocarbonyl, alkynylthiocarbonyl, arylthiocarbonyl, alkyloxythiocarbonyl, alkenyloxythiocarbonyl, alkynyloxythiocarbonyl, aryloxythiocarbonyl, alkylaminothiocarbonyl, alkenylaminothiocarbonyl, alkynylaminothiocarbonyl, arylaminothiocarbonyl, alkylthiothiocarbonyl, alkenylthiothiocarbonyl, alkynylthiothiocarbonyl, arylthiothiocarbonyl, provided that at least one of R^3, R^{10}, R^{11}, or R^{12} is not hydrogen when R^2 is $-C(=O)NR^2R^{2'}$ and $R^{12'}$ is OR^{12};

R^4 and $R^{4'}$ are each independently $NR^{4a}R^{4b}$, alkyl, alkenyl, alkynyl, hydroxyl, halogen, hydrogen, or when taken together the oxygen of a carbonyl group;

R^5 is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^6 and $R^{6'}$ are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{8c}C(=E')ER^{8a}$;

R^9 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{9c}C(=Z')ZR^{9a}$;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, and R^{8f} are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$R^{12'}$ is OR^{12} or $NR^{12}R^{12''}$;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

E is $CR^{8d}R^{8e}$, S, NR^{8b} or O;

E' is O, NR^{8f}, or S;

W is $CR^{7d}R^{7e}$, S, NR^{7b} or O;

W' is O, NR^{7f}, or S;

X is $CHC(R^{13}Y'Y)$, $C{=}CR^{13}Y$, $CR^{6'}R^6$, S, NR^6, or O;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

Z is $CR^{9d}R^{9e}$, S, NR^{9b} or O;

Z' is O, S, or NR^{9f}, and pharmaceutically acceptable salts, esters and enantiomers thereof.

2. The tetracycline compound of claim 1, wherein X is $CR^6R^{6'}$; R^2, $R^{2'}$, R^6, $R^{6'}$, R^8 and R^{11} are each hydrogen; and R^5 is hydroxy or hydrogen.

3. The tetracycline compound of claim 2, wherein R^4 is dialkylamino, and $R^{4'}$ and R^5 are each hydrogen.

4. The tetracycline compound of any one of claims 1-3, wherein R^3 is alkyl, alkenyl, aryl, acetyl, aralkyl, alkynyl, alkylcarbonyl, alkenylcarbonyl, arylcarbonyl, alkynylcarbonyl, alkyloxycarbonyl, alkenyloxycarbonyl, alkynyloxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl. alkynylaminocarbonyl, arylaminocarbonyl, alkylthiocarbonyl, alkenylthiocarbonyl, alkynylthiocarbonyl, arylthiocarbonyl, alkyloxythiocarbonyl, alkenyloxythiocarbonyl, alkynyloxythiocarbonyl, aryloxythiocarbonyl, alkylaminothiocarbonyl,

alkenylaminothiocarbonyl, alkynylaminothiocarbonyl, arylaminothiocarbonyl, alkylthiothiocarbonyl, alkenylthiothiocarbonyl, alkynylthiothiocarbonyl, or arylthiothiocarbonyl.

5. The tetracycline compound of claim 4, wherein R^3 is aralkyl.

6. The tetracycline compound of claim 5, wherein R^3 is benzyl.

7. The tetracycline compound of claim 4, wherein R^3 is alkyl.

8. The tetracycline compound of claim 4, wherein R^3 is acetyl.

9. The tetracycline compound of claim 4, wherein R^3 is alkenyl.

10. The tetracycline compound of claims 1-3, wherein R^3 is hydrogen.

11. The tetracycline compound of claim 4, wherein R^{10} alkyl, alkenyl, aryl, acetyl, aralkyl, alkynyl, alkylcarbonyl, alkenylcarbonyl, arylcarbonyl, alkynylcarbonyl, alkyloxycarbonyl, alkenyloxycarbonyl, alkynyloxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkynylaminocarbonyl, arylaminocarbonyl, alkylthiocarbonyl, alkenylthiocarbonyl, alkynylthiocarbonyl, arylthiocarbonyl, alkyloxythiocarbonyl, alkenyloxythiocarbonyl, alkynyloxythiocarbonyl, aryloxythiocarbonyl, alkylaminothiocarbonyl, alkenylaminothiocarbonyl, alkynylaminothiocarbonyl, arylaminothiocarbonyl, alkylthiothiocarbonyl, alkenylthiothiocarbonyl, alkynylthiothiocarbonyl, or arylthiothiocarbonyl.

12. The tetracycline compound of claim 11, wherein R^{10} is aralkyl.

13. The tetracycline compound of claim 12, wherein R^{10} is benzyl.

14. The tetracycline compound of claim 11, wherein R^{10} is alkyl.

15. The tetracycline compound of claim 11, wherein R^{10} is acetyl.

16. The tetracycline compound of claim 11, wherein R^{10} is alkenyl.

17. The tetracycline compound of claim 1, wherein R^{10} is hydrogen.

18. The tetracycline compound of claim 1, wherein R^{12} is alkyl, alkenyl, aryl, acetyl, aralkyl, alkynyl, alkylcarbonyl, alkenylcarbonyl, arylcarbonyl, alkynylcarbonyl, alkyloxycarbonyl, alkenyloxycarbonyl, alkynyloxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, alkenylaminocarbonyl, alkynylaminocarbonyl, arylaminocarbonyl, alkylthiocarbonyl, alkenylthiocarbonyl, alkynylthiocarbonyl, arylthiocarbonyl, alkyloxythiocarbonyl, alkenyloxythiocarbonyl, alkynyloxythiocarbonyl, aryloxythiocarbonyl, alkylaminothiocarbonyl, alkenylaminothiocarbonyl, alkynylaminothiocarbonyl, arylaminothiocarbonyl, alkylthiothiocarbonyl, alkenylthiothiocarbonyl, alkynylthiothiocarbonyl, or arylthiothiocarbonyl.

19. The tetracycline compound of claim 18, wherein R^{12} is aralkyl.

20. The tetracycline compound of claim 19, wherein R^{12} is benzyl.

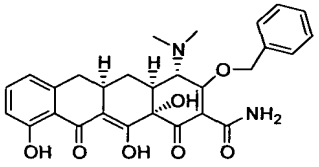
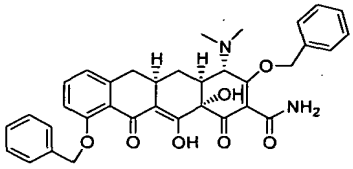
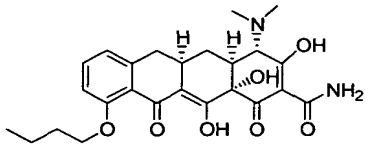
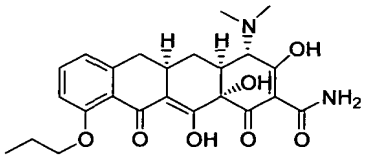
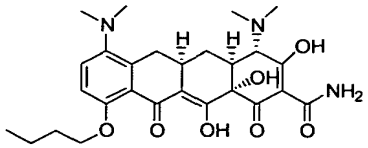
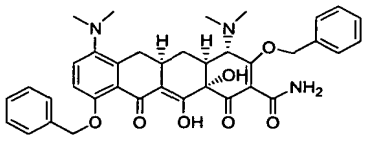
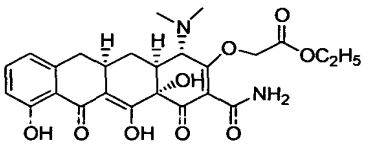
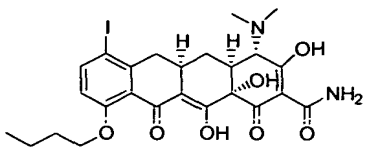
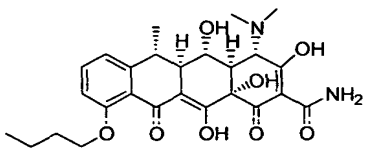
21. The tetracycline compound of claim 18, wherein R^{12} is alkyl.

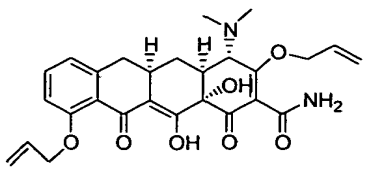
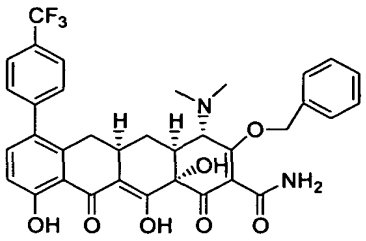
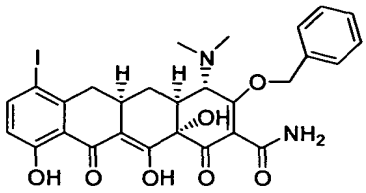
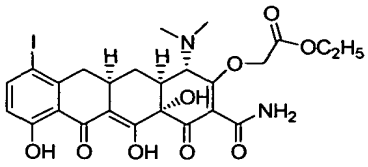
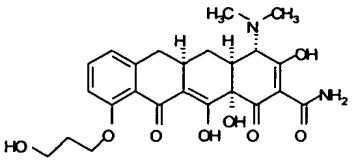
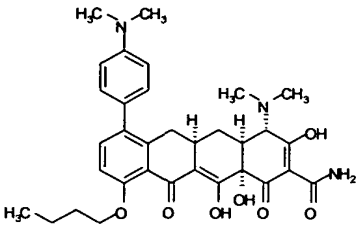
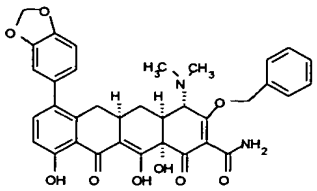
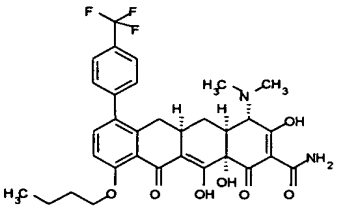
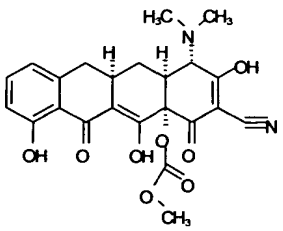
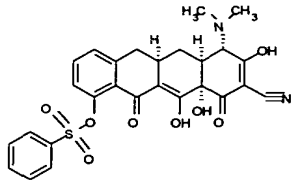
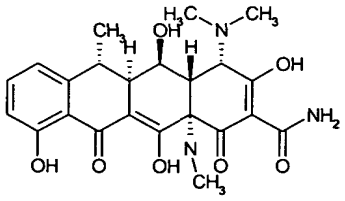
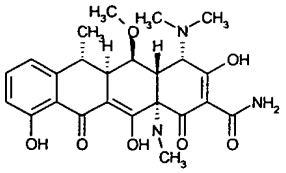
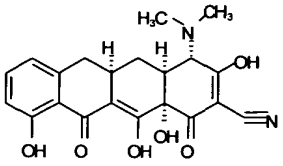
22. The tetracycline compound of claim 18, wherein R^{12} is acetyl.

23. The tetracycline compound of claim 18, wherein R^{12} is alkenyl.

24. The tetracycline compound of claim 1, wherein R^{12} is hydrogen.

25. A tetracycline compound selected from the group consisting of:

26. A method for treating a tetracycline responsive state in a subject, comprising administering to said subject a tetracycline compound of claim 1 or 25, such that said tetracycline responsive state is treated.

27. The method of claim 26, wherein said subject is a human.

28. The method of claim 26, wherein said tetracycline compound is non-antibacterial.

29. The method of claim 26 wherein said tetracycline responsive state is an inflammatory process associated state.

30. The method of claim 26, wherein said tetracycline responsive state is cancer.

31. The method of claim 26, wherein said tetracycline responsive state is lung injury.

32. The method of claim 26, wherein said tetracycline responsive state is an eye disorder.

33. The method of claim 26, wherein said tetracycline responsive state is stroke.

34. The method of claim 26, wherein said tetracycline responsive state is a neurological disorder.

35. The method of claim 34, wherein said neurological disorder is Alzheimer's disease, Huntington's disease, Parkinson's disease, amylotropic lateral sclerosis, or multiple sclerosis.

36. A pharmaceutical composition comprising a therapeutically effective amount of a tetracycline compound of claim 1 or 25, and a pharmaceutically acceptable carrier.